IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: GARABEDIAN=2A

In re Application of:	)	Art Unit: 1647
Michael GARABEDIAN	)	Examiner: Daniel C. Gamett
Appln. No.: 10/629,913	)	Washington, D.C.
Date Filed: July 30, 2003	)	Confirmation No. 8615
For: ANTIBODIES THAT RECOGNIZE AND BIND PHOSPHORYLATED…	)	

DECLARATION UNDER 37 CFR §1.132

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window
Randolph Building, Mail Stop
401 Dulany Street
Alexandria, VA 22314

Sir:

We, Michael Garabedian and Zhen Wang, hereby declare and state as follows:

We are the same Michael Garabedian and Zhen Wang who are the co-inventors of the invention(s) disclosed and claimed in the above-identified application no. 10/629,913.

We are also the same Michael Garabedian and Zhen Wang who are listed among the co-authors of the publication, Wang, Z., Frederick, J. and Garabedian, M. "Deciphering the Phosphorylation 'Code' of the Glucocorticoid Receptor *In Vivo*" *J. Biol. Chem.* 277(29):26573-26580 (2002).

Also listed as co-author on the above publication was Jeremy Frederick. While Jeremy Frederick was a co-author and a co-worker with us, he was not involved in the conception and is not a co-inventor of the invention(s) claimed in the above-identified application no. 10/629,913.

The undersigned declare further that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

4/21/05
Date

Michael GARABEDIAN

4/20/2005
Date

Zhen WANG

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1: P04150. Reports Glucocorticoid re...[gi:121069]


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LOCUS       P04150                  777 aa            linear   PRI 01-MAY-2005
DEFINITION  Glucocorticoid receptor (GR).
ACCESSION   P04150
VERSION     P04150  GI:121069
DBSOURCE    swissprot: locus GCR_HUMAN, accession P04150;
            class: standard.
            extra accessions:P04151,created: Nov 1, 1986.
            sequence updated: Nov 1, 1986.
            annotation updated: May 1, 2005.
            xrefs: X03225.1, CAA26976.1, X03348.1, CAA27054.1, U80946.1,
            AAB64353.1, U78506.1, U78507.1, U78508.1, U78509.1, U78510.1,
            U78511.1, U78512.1, U80947.1, AAB64354.1, U01351.1, AAA16603.1,
            AY436590.1, AAQ97180.1, BC015610.2, AAH15610.1, M69104.1,
            AAA88049.1, M73816.1, AAA53151.1, S68378.1, AAB20466.1, AC005601.1,
            AAC34207.1, QRHUGA, QRHUGB, 1M2ZA, 1M2ZD, 1NHZA, 1P93A, 1P93B,
            1P93C, 1P93D
            xrefs (non-sequence databases): SMRP04150, IntActP04150,
            TRANSFACT00337, TRANSFACT01920, EnsemblENSG00000113580,
            GenewHGNC:7978, H-InvDBHIX0005273, MIM 138040, GO0005737,
            GO0005759, GO0005634, GO0004883, GO0003700, GO0007165, GO0006366,
            InterProIPR001409, InterProIPR000536, InterProIPR001723,
            InterProIPR008946, InterProIPR001628, PfamPF02155, PfamPF00104,
            PfamPF00105, PRINTSPR00528, PRINTSPR00398, PRINTSPR00047,
            ProDomPD000035, SMARTSM00430, SMARTSM00399, PROSITEPS00031,
            PROSITEPS51030
KEYWORDS    3D-structure; Alternative initiation; Alternative splicing; Disease
            mutation; DNA-binding; Metal-binding; Nuclear protein;
            Phosphorylation; Polymorphism; Receptor; Steroid-binding;
            Trans-acting factor; Transcription; Transcription regulation; Ubl
            conjugation; Zinc; Zinc-finger.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (residues 1 to 777)
  AUTHORS   Hollenberg,S.M., Weinberger,C., Ong,E.S., Cerelli,G., Oro,A.,
            Lebo,R., Thompson,E.B., Rosenfeld,M.G. and Evans,R.M.
  TITLE     Primary structure and expression of a functional human
            glucocorticoid receptor cDNA
  JOURNAL   Nature 318 (6047), 635-641 (1985)
   PUBMED   2867473
  REMARK    NUCLEOTIDE SEQUENCE [MRNA] (ISOFORMS ALPHA AND BETA).
            TISSUE=Fibroblast
REFERENCE   2  (residues 1 to 777)
  AUTHORS   Encio,I.J. and Detera-Wadleigh,S.D.
  TITLE     The genomic structure of the human glucocorticoid receptor
  JOURNAL   J. Biol. Chem. 266 (11), 7182-7188 (1991)
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PUBMED 1707881
REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORMS ALPHA AND BETA).
REFERENCE 3 (residues 1 to 777)
AUTHORS Munroe,D.G., Pang,J., Taylor,G.R., Lau,C., Plante,R.K. and Zhou,L.
TITLE Direct Submission
JOURNAL Submitted (??-SEP-1993)
REMARK NUCLEOTIDE SEQUENCE [MRNA] (ISOFORM GAMMA).
REFERENCE 4 (residues 1 to 777)
AUTHORS Rieder,M.J., Livingston,R.J., Daniels,M.R., Chung,M.-W., Miyamoto,K.E., Nguyen,C.P., Nguyen,D.A., Poel,C.L., Robertson,P.D., Schackwitz,W.S., Sherwood,J.K., Witrak,L.A. and Nickerson,D.A.
TITLE Direct Submission
JOURNAL Submitted (??-OCT-2003)
REMARK NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM ALPHA), AND VARIANTS LYS-23 AND VAL-65.
REFERENCE 5 (residues 1 to 777)
AUTHORS Strausberg,R.L., Feingold,E.A., Grouse,L.H., Derge,J.G., Klausner,R.D., Collins,F.S., Wagner,L., Shenmen,C.M., Schuler,G.D., Altschul,S.F., Zeeberg,B., Buetow,K.H., Schaefer,C.F., Bhat,N.K., Hopkins,R.F., Jordan,H., Moore,T., Max,S.I., Wang,J., Hsieh,F., Diatchenko,L., Marusina,K., Farmer,A.A., Rubin,G.M., Hong,L., Stapleton,M., Soares,M.B., Bonaldo,M.F., Casavant,T.L., Scheetz,T.E., Brownstein,M.J., Usdin,T.B., Toshiyuki,S., Carninci,P., Prange,C., Raha,S.S., Loquellano,N.A., Peters,G.J., Abramson,R.D., Mullahy,S.J., Bosak,S.A., McEwan,P.J., McKernan,K.J., Malek,J.A., Gunaratne,P.H., Richards,S., Worley,K.C., Hale,S., Garcia,A.M., Gay,L.J., Hulyk,S.W., Villalon,D.K., Muzny,D.M., Sodergren,E.J., Lu,X., Gibbs,R.A., Fahey,J., Helton,E., Ketteman,M., Madan,A., Rodrigues,S., Sanchez,A., Whiting,M., Madan,A., Young,A.C., Shevchenko,Y., Bouffard,G.G., Blakesley,R.W., Touchman,J.W., Green,E.D., Dickson,M.C., Rodriguez,A.C., Grimwood,J., Schmutz,J., Myers,R.M., Butterfield,Y.S., Krzywinski,M.I., Skalska,U., Smailus,D.E., Schnerch,A., Schein,J.E., Jones,S.J. and Marra,M.A.
CONSRTM Mammalian Gene Collection Program Team
TITLE Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 99 (26), 16899-16903 (2002)
PUBMED 12477932
REMARK NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM ALPHA). TISSUE=Placenta
REFERENCE 6 (residues 1 to 777)
AUTHORS Leclerc,S., Xie,B.X., Roy,R. and Govindan,M.V.
TITLE Purification of a human glucocorticoid receptor gene promoter-binding protein. Production of polyclonal antibodies against the purified factor
JOURNAL J. Biol. Chem. 266 (14), 8711-8719 (1991)
PUBMED 2026589
REMARK NUCLEOTIDE SEQUENCE OF 1-394.
REFERENCE 7 (residues 1 to 777)
AUTHORS Govindan,M.V., Pothier,F., Leclerc,S., Palaniswami,R. and Xie,B.
TITLE Human glucocorticoid receptor gene promotor-homologous down regulation
JOURNAL J. Steroid Biochem. Mol. Biol. 40 (1-3), 317-323 (1991)
PUBMED 1958537
REMARK NUCLEOTIDE SEQUENCE OF 1-394.
REFERENCE 8 (residues 1 to 777)
AUTHORS Kimmerly,W., Bondoc,M., Cheng,J., Connolly,K.S., Gunning,K.M., Kadner,K., Miguel,T., Miller,C., Pitluck,S., Pollard,M., Rojeski,H., Subramanian,S. and Martin,C.H.
TITLE Direct Submission
JOURNAL Submitted (??-SEP-1998)
REMARK NUCLEOTIDE SEQUENCE OF 396-630.
REFERENCE 9 (residues 1 to 777)
AUTHORS Yudt,M.R. and Cidlowski,J.A.
TITLE Molecular identification and characterization of a and b forms of the glucocorticoid receptor

JOURNAL Mol. Endocrinol. 15 (7), 1093-1103 (2001)
PUBMED 11435610
REMARK ALTERNATIVE INITIATION, AND MUTAGENESIS OF MET-1 AND MET-27.
REFERENCE 10 (residues 1 to 777)
AUTHORS Weinberger,C., Hollenberg,S.M., Rosenfeld,M.G. and Evans,R.M.
TITLE Domain structure of human glucocorticoid receptor and its relationship to the v-erb-A oncogene product
JOURNAL Nature 318 (6047), 670-672 (1985)
PUBMED 3841189
REMARK DOMAINS.
REFERENCE 11 (residues 1 to 777)
AUTHORS Henriksson,A., Almlof,T., Ford,J., McEwan,I.J., Gustafsson,J.A. and Wright,A.P.
TITLE Role of the Ada adaptor complex in gene activation by the glucocorticoid receptor
JOURNAL Mol. Cell. Biol. 17 (6), 3065-3073 (1997)
PUBMED 9154805
REMARK INTERACTIONS WITH TADA2L AND THE ADA COMPLEX, AND MUTAGENESIS OF PHE-191; ILE-193; LEU-194; LEU-197; TRP-213; LEU-224; LEU-225; PHE-235 AND LEU-236.
REFERENCE 12 (residues 1 to 777)
AUTHORS Fryer,C.J. and Archer,T.K.
TITLE Chromatin remodelling by the glucocorticoid receptor requires the BRG1 complex
JOURNAL Nature 393 (6680), 88-91 (1998)
PUBMED 9590696
REMARK INTERACTIONS WITH THE SMARCA4 COMPLEX; NCOA1; NCOA2 AND THE CREBBP/EP300 COMPLEX.
REFERENCE 13 (residues 1 to 777)
AUTHORS Schneikert,J., Hubner,S., Martin,E. and Cato,A.C.
TITLE A nuclear action of the eukaryotic cochaperone RAP46 in downregulation of glucocorticoid receptor activity
JOURNAL J. Cell Biol. 146 (5), 929-940 (1999)
PUBMED 10477749
REMARK INTERACTION WITH BAG1.
REFERENCE 14 (residues 1 to 777)
AUTHORS Rivers,C., Levy,A., Hancock,J., Lightman,S. and Norman,M.
TITLE Insertion of an amino acid in the DNA-binding domain of the glucocorticoid receptor as a result of alternative splicing
JOURNAL J. Clin. Endocrinol. Metab. 84 (11), 4283-4286 (1999)
PUBMED 10566686
REMARK ALTERNATIVE SPLICING (ISOFORM GAMMA).
REFERENCE 15 (residues 1 to 777)
AUTHORS Moalli,P.A., Pillay,S., Krett,N.L. and Rosen,S.T.
TITLE Alternatively spliced glucocorticoid receptor messenger RNAs in glucocorticoid-resistant human multiple myeloma cells
JOURNAL Cancer Res. 53 (17), 3877-3879 (1993)
PUBMED 8358712
REMARK ALTERNATIVE SPLICING (ISOFORMS GP-P AND GP-A).
REFERENCE 16 (residues 1 to 777)
AUTHORS Lu,N.Z. and Cidlowski,J.A.
TITLE The origin and functions of multiple human glucocorticoid receptor isoforms
JOURNAL Ann. N. Y. Acad. Sci. 1024, 102-123 (2004)
PUBMED 15265776
REMARK REVIEW ON ALTERNATIVE SPLICING, ALTERNATIVE INITIATION, AND POSTTRANSLATIONAL MODIFICATIONS.
REFERENCE 17 (residues 1 to 777)
AUTHORS Mahajan,M.A. and Samuels,H.H.
TITLE A new family of nuclear receptor coregulators that integrate nuclear receptor signaling through CREB-binding protein
JOURNAL Mol. Cell. Biol. 20 (14), 5048-5063 (2000)
PUBMED 10866662
REMARK INTERACTION WITH NCOA6.
REFERENCE 18 (residues 1 to 777)
AUTHORS Wallace,A.D. and Cidlowski,J.A.
TITLE Proteasome-mediated glucocorticoid receptor degradation restricts

transcriptional signaling by glucocorticoids
JOURNAL J. Biol. Chem. 276 (46), 42714-42721 (2001)
PUBMED 11555652
REMARK GLUCOCORTICOID-MEDIATED DOWN-REGULATION.
REFERENCE 19 (residues 1 to 777)
AUTHORS Tian,S., Poukka,H., Palvimo,J.J. and Janne,O.A.
TITLE Small ubiquitin-related modifier-1 (SUMO-1) modification of the glucocorticoid receptor
JOURNAL Biochem. J. 367 (PT 3), 907-911 (2002)
PUBMED 12144530
REMARK SUMOYLATION, AND MUTAGENESIS OF LYS-277; LYS-293 AND LYS-703.
REFERENCE 20 (residues 1 to 777)
AUTHORS Wang,Z., Frederick,J. and Garabedian,M.J.
TITLE Deciphering the phosphorylation 'code' of the glucocorticoid receptor in vivo
JOURNAL J. Biol. Chem. 277 (29), 26573-26580 (2002)
PUBMED 12000743
REMARK PHOSPHORYLATION SITES SER-203 AND SER-211.
REFERENCE 21 (residues 1 to 777)
AUTHORS Bledsoe,R.K., Montana,V.G., Stanley,T.B., Delves,C.J., Apolito,C.J., McKee,D.D., Consler,T.G., Parks,D.J., Stewart,E.L., Willson,T.M., Lambert,M.H., Moore,J.T., Pearce,K.H. and Xu,H.E.
TITLE Crystal structure of the glucocorticoid receptor ligand binding domain reveals a novel mode of receptor dimerization and coactivator recognition
JOURNAL Cell 110 (1), 93-105 (2002)
PUBMED 12151000
REMARK X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS) OF 521-777 OF MUTANT SER-602 IN COMPLEX WITH NCOA2; DEXAMETHASONE AND RU-486, AND MUTAGENESIS OF ARG-585; ASP-590; PHE-602; PRO-625 AND ILE-628.
REFERENCE 22 (residues 1 to 777)
AUTHORS Kauppi,B., Jakob,C., Farnegardh,M., Yang,J., Ahola,H., Alarcon,M., Calles,K., Engstrom,O., Harlan,J., Muchmore,S., Ramqvist,A.K., Thorell,S., Ohman,L., Greer,J., Gustafsson,J.A., Carlstedt-Duke,J. and Carlquist,M.
TITLE The three-dimensional structures of antagonistic and agonistic forms of the glucocorticoid receptor ligand-binding domain: RU-486 induces a transconformation that leads to active antagonism
JOURNAL J. Biol. Chem. 278 (25), 22748-22754 (2003)
PUBMED 12686538
REMARK X-RAY CRYSTALLOGRAPHY (2.3 ANGSTROMS) OF 500-777 OF MUTANT SER-602 IN COMPLEX WITH COACTIVATOR PEPTIDE; DEXAMETHASONE AND WITH RU-486.
REFERENCE 23 (residues 1 to 777)
AUTHORS Hurley,D.M., Accili,D., Stratakis,C.A., Karl,M., Vamvakopoulos,N., Rorer,E., Constantine,K., Taylor,S.I. and Chrousos,G.P.
TITLE Point mutation causing a single amino acid substitution in the hormone binding domain of the glucocorticoid receptor in familial glucocorticoid resistance
JOURNAL J. Clin. Invest. 87 (2), 680-686 (1991)
PUBMED 1704018
REMARK CHARACTERIZATION OF VARIANT GLUCOCORTICOID RESISTANCE VAL-641.
REFERENCE 24 (residues 1 to 777)
AUTHORS Powers,J.H., Hillmann,A.G., Tang,D.C. and Harmon,J.M.
TITLE Cloning and expression of mutant glucocorticoid receptors from glucocorticoid-sensitive and -resistant human leukemic cells
JOURNAL Cancer Res. 53 (17), 4059-4065 (1993)
PUBMED 8358735
REMARK VARIANTS TYR-421 AND PHE-753.
REFERENCE 25 (residues 1 to 777)
AUTHORS Karl,M., Lamberts,S.W., Detera-Wadleigh,S.D., Encio,I.J., Stratakis,C.A., Hurley,D.M., Accili,D. and Chrousos,G.P.
TITLE Familial glucocorticoid resistance caused by a splice site deletion in the human glucocorticoid receptor gene
JOURNAL J. Clin. Endocrinol. Metab. 76 (3), 683-689 (1993)
PUBMED 8445027
REMARK VARIANT SER-363.
REFERENCE 26 (residues 1 to 777)

AUTHORS Malchoff,D.M., Brufsky,A., Reardon,G., McDermott,P., Javier,E.C., Bergh,C.H., Rowe,D. and Malchoff,C.D.
TITLE A mutation of the glucocorticoid receptor in primary cortisol resistance
JOURNAL J. Clin. Invest. 91 (5), 1918-1925 (1993)
PUBMED 7683692
REMARK VARIANT GLUCOCORTICOID RESISTANCE ILE-729.
REFERENCE 27 (residues 1 to 777)
AUTHORS Ashraf,J. and Thompson,E.B.
TITLE Identification of the activation-labile gene: a single point mutation in the human glucocorticoid receptor presents as two distinct receptor phenotypes
JOURNAL Mol. Endocrinol. 7 (5), 631-642 (1993)
PUBMED 8316249
REMARK VARIANT PHE-753.
REFERENCE 28 (residues 1 to 777)
AUTHORS Koper,J.W., Stolk,R.P., de Lange,P., Huizenga,N.A.T.M., Molijn,G.-J., Pols,H.A.P., Grobbee,D.E., Karl,M., de Jong,F.H., Brinkmann,A.O. and Lamberts,S.W.J.
TITLE Lack of association between five polymorphisms in the human glucocorticoid receptor gene and glucocorticoid resistance
JOURNAL Hum. Genet. 99 (5), 663-668 (1997)
PUBMED 9150737
REMARK VARIANTS LYS-23 AND SER-363.
REFERENCE 29 (residues 1 to 777)
AUTHORS Cargill,M., Altshuler,D., Ireland,J., Sklar,P., Ardlie,K., Patil,N., Shaw,N., Lane,C.R., Lim,E.P., Kalyanaraman,N., Nemesh,J., Ziaugra,L., Friedland,L., Rolfe,A., Warrington,J., Lipshutz,R., Daley,G.Q. and Lander,E.S.
TITLE Characterization of single-nucleotide polymorphisms in coding regions of human genes
JOURNAL Nat. Genet. 22 (3), 231-238 (1999)
PUBMED 10391209
REMARK VARIANTS LYS-23; VAL-65 AND SER-363.
REFERENCE 30 (residues 1 to 777)
AUTHORS Cargill,M., Altshuler,D., Ireland,J., Sklar,P., Ardlie,K., Patil,N., Shaw,N., Lane,C.R., Lim,E.P., Kalyanaraman,N., Nemesh,J., Ziaugra,L., Friedland,L., Rolfe,A., Warrington,J., Lipshutz,R., Daley,G.Q. and Lander,E.S.
JOURNAL Nat. Genet. 23, 373-373 (1999)
REMARK ERRATUM.
REFERENCE 31 (residues 1 to 777)
AUTHORS Feng,J., Zheng,J., Bennett,W.P., Heston,L.L., Jones,I.R., Craddock,N. and Sommer,S.S.
TITLE Five missense variants in the amino-terminal domain of the glucocorticoid receptor: no association with puerperal psychosis or schizophrenia
JOURNAL Am. J. Med. Genet. 96 (3), 412-417 (2000)
PUBMED 10898924
REMARK VARIANTS LYS-23; LEU-29; PHE-112; ASN-233 AND SER-363.
REFERENCE 32 (residues 1 to 777)
AUTHORS Ruiz,M., Lind,U., Gafvels,M., Eggertsen,G., Carlstedt-Duke,J., Nilsson,L., Holtmann,M., Stierna,P., Wikstrom,A.C. and Werner,S.
TITLE Characterization of two novel mutations in the glucocorticoid receptor gene in patients with primary cortisol resistance
JOURNAL Clin. Endocrinol. (Oxf) 55 (3), 363-371 (2001)
PUBMED 11589680
REMARK VARIANTS GLUCOCORTICOID RESISTANCE HIS-477 AND SER-679.
REFERENCE 33 (residues 1 to 777)
AUTHORS Kino,T., Stauber,R.H., Resau,J.H., Pavlakis,G.N. and Chrousos,G.P.
TITLE Pathologic human GR mutant has a transdominant negative effect on the wild-type GR by inhibiting its translocation into the nucleus: importance of the ligand-binding domain for intracellular GR trafficking
JOURNAL J. Clin. Endocrinol. Metab. 86 (11), 5600-5608 (2001)
PUBMED 11701741
REMARK CHARACTERIZATION OF VARIANT GLUCOCORTICOID RESISTANCE ASN-559.

REFERENCE 34 (residues 1 to 777)
AUTHORS Vottero,A., Kino,T., Combe,H., Lecomte,P. and Chrousos,G.P.
TITLE A novel, C-terminal dominant negative mutation of the GR causes familial glucocorticoid resistance through abnormal interactions with p160 steroid receptor coactivators
JOURNAL J. Clin. Endocrinol. Metab. 87 (6), 2658-2667 (2002)
PUBMED 12050230
REMARK VARIANT GLUCOCORTICOID RESISTANCE MET-747, AND ALTERED INTERACTION WITH THE COACTIVATOR NCOA2.

COMMENT On or before Mar 15, 2005 this sequence version replaced gi:72116, gi:72117, gi:121070.
[FUNCTION] Receptor for glucocorticoids (GC). Has a dual mode of action: as a transcription factor that binds to glucocorticoid response elements (GRE) and as a modulator of other transcription factors. Affects inflammatory responses, cellular proliferation and differentiation in target tissues.
[SUBUNIT] Heteromultimeric cytoplasmic complex with HSP90, HSP70, and FKBP5 or another immunophilin, or the immunophilin homolog PPP5C. Upon ligand binding FKBP5 dissociates from the complex and FKBP4 takes its place, thereby linking the complex to dynein and mediating transport to the nucleus, where the complex dissociates (By similarity). Binds to DNA as a homodimer, and as a heterodimer with NR3C2 or the retinoid X receptor. Binds STAT5A and STAT5B homodimers and heterodimers. Interacts with NRIP1, POU2F1, POU2F2 and TRIM28 (By similarity). Interacts with several coactivator complexes, including the SMARCA4 complex, CREBBP/EP300, TADA2L and p160 coactivators such as NCOA2 and NCOA6. Interaction with BAG1 inhibits transactivation.
[INTERACTION] P51532:SMARCA4; NbExp=1; IntAct=EBI-493507, EBI-302489; Q92922:SMARCC1; NbExp=1; IntAct=EBI-493507, EBI-355653.
[SUBCELLULAR LOCATION] Cytoplasmic in the absence of ligand; nuclear after ligand-binding.
[ALTERNATIVE PRODUCTS] Event=Alternative splicing; Named isoforms=5; Comment=Additional isoforms seem to exist; Name=Alpha; Synonyms=Alpha-A; IsoId=P04150-1; Sequence=Displayed; Note=Predominant physiological form. Isoform Alpha-B is produced by alternative initiation at Met-27 of isoform Alpha. Both isoforms exhibit similar subcellular location and nuclear translocation after ligand activation. Isoform Alpha-B appears to be more susceptible to degradation, at least when expressed in mammalian cells, but more effective in transcriptional activation and not in transrepression; Name=Beta; Synonyms=Beta-A; IsoId=P04150-2; Sequence=VSP_003703; Note=No hormone-binding activity. Widely expressed at low level. Localized largely in the nucleus. Isoform Beta-B is produced by alternative initiation at Met-27 of isoform Beta; Name=Gamma; Synonyms=Alpha-2, Gamma-A, Alpha-2-A; IsoId=P04150-3; Sequence=VSP_007363; Note=Lower transcriptional activity. Expressed at low level; Name=GR-P; IsoId=P04150-4; Sequence=Not described; Note=Encoded by exons 2-7 plus several basepairs from the subsequent intron region. Lacks the ligand binding domain. Accounts for up to 10-20% of mRNAs; Name=GR-A; IsoId=P04150-5; Sequence=VSP_013340; Note=Lacks exons 5, 6 and 7. Found in glucocorticoid-resistant myeloma patients; Event=Alternative initiation; Comment=At least 4 isoforms, Alpha (shown here), Alpha-B, Beta and Beta-B, are produced by alternative initiation at Met-1 and Met-27. The existence of isoform Alpha and isoform Alpha-B has been proved by mutagenesis. As the sequence environment of the 2 potential ATG initiator codons is the same for the other isoforms, alternative initiation of translation could also occur on these transcripts.
[TISSUE SPECIFICITY] Widely expressed.
[DOMAIN] Composed of three domains: a modulating N-terminal domain, a DNA-binding domain and a C-terminal steroid-binding domain.
[PTM] Increased proteasome-mediated degradation in response to glucocorticoids.
[PTM] Phosphorylated in the absence of hormone; becomes hyperphosphorylated in the presence of glucocorticoid. The

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            Ser-203-phosphorylated form is mainly cytoplasmic, and the
            Ser-211-phosphorylated form is nuclear. Transcriptional activity
            correlates with the amount of phosphorylation at Ser-211.
            [PTM] Sumoylated; this reduces transcription transactivation.
            [DISEASE] Defects in NR3C1 are a cause of glucocorticoid resistance
            [MIM:138040]; also known as cortisol resistance. It is a
            hypertensive, hyperandrogenic disorder characterized by increased
            serum cortisol concentrations. Inheritance is autosomal dominant.
            [SIMILARITY] Belongs to the nuclear hormone receptor family. NR3
            subfamily.
            [SIMILARITY] Contains 1 nuclear receptor DNA-binding domain.
FEATURES             Location/Qualifiers
     source          1..777
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
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                     /gene="NR3C1"
                     /note="synonym: GRL"
     Protein         1..777
                     /gene="NR3C1"
                     /product="Glucocorticoid receptor"
     Region          1..777
                     /gene="NR3C1"
                     /region_name="Mature chain"
                     /note="Glucocorticoid receptor, A-type isoforms."
                     /evidence=experimental
     Region          1..420
                     /gene="NR3C1"
                     /region_name="Domain"
                     /note="Modulating."
                     /evidence=experimental
     Site            1
                     /gene="NR3C1"
                     /site_type="mutagenized"
                     /note="M->T: Abolishes expression of A-type isoforms."
                     /evidence=experimental
     Region          23
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="R -> K (in dbSNP:6190). /FTId=VAR_014140."
                     /evidence=experimental
     Region          27..777
                     /gene="NR3C1"
                     /region_name="Mature chain"
                     /note="Glucocorticoid receptor, B-type isoforms."
                     /evidence=experimental
     Site            27
                     /gene="NR3C1"
                     /site_type="mutagenized"
                     /note="M->T: Abolishes expression of B-type isoforms."
                     /evidence=experimental
     Region          29
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="F -> L. /FTId=VAR_015628."
                     /evidence=experimental
     Region          65
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="F -> V (in dbSNP:6192). /FTId=VAR_014622."
                     /evidence=experimental
     Region          112
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="L -> F. /FTId=VAR_015629."
                     /evidence=experimental
     Site            113
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                /gene="NR3C1"
                /site_type="modified"
                /note="Phosphoserine (By similarity)."
                /evidence=not_experimental
     Site       141
                /gene="NR3C1"
                /site_type="modified"
                /note="Phosphoserine (By similarity)."
                /evidence=not_experimental
     Site       191
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="F->D: Reduces transactivation by the ADA complex."
                /evidence=experimental
     Site       193
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="I->D: Reduces transactivation by the ADA complex."
                /evidence=experimental
     Site       194
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="L->A: Strongly reduces transactivation by the ADA
                complex; when associated with V- 224 and F-225."
                /evidence=experimental
     Site       197
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="L->E: Reduces transactivation by the ADA complex."
                /evidence=experimental
     Site       203
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                /site_type="modified"
                /note="Phosphoserine."
                /evidence=experimental
     Site       211
                /gene="NR3C1"
                /site_type="modified"
                /note="Phosphoserine."
                /evidence=experimental
     Site       213
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="W->A: Strongly reduces transactivation by the ADA
                complex."
                /evidence=experimental
     Site       224
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="L->V: Strongly reduces transactivation by the ADA
                complex; when associated with A- 194 and F-225."
                /evidence=experimental
     Site       225
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="L->F: Strongly reduces transactivation by the ADA
                complex; when associated with A- 194 and V-224."
                /evidence=experimental
     Site       226
                /gene="NR3C1"
                /site_type="modified"
                /note="Phosphoserine (By similarity)."
                /evidence=not_experimental
     Region     233
                /gene="NR3C1"
                /region_name="Variant"
                /note="D -> N. /FTId=VAR_015630."
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                     /evidence=experimental
     Site            235
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                     /site_type="mutagenized"
                     /note="F->L: Strongly reduces transactivation by the ADA
                     complex; when associated with V- 236."
                     /evidence=experimental
     Site            236
                     /gene="NR3C1"
                     /site_type="mutagenized"
                     /note="L->V: Strongly reduces transactivation by the ADA
                     complex; when associated with L- 235."
                     /evidence=experimental
     Site            277
                     /gene="NR3C1"
                     /site_type="mutagenized"
                     /note="K->R: Strongly reduces sumoylation. Almost complete
                     loss of sumoylation; when associated with R-293."
                     /evidence=experimental
     Site            293
                     /gene="NR3C1"
                     /site_type="mutagenized"
                     /note="K->R: Strongly reduces sumoylation. Almost complete
                     loss of sumoylation; when associated with R-277."
                     /evidence=experimental
     Region          363
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="N -> S (may increase sensitivity to exogenously
                     administered glucocorticoids; dbSNP:6195).
                     /FTId=VAR_004675."
                     /evidence=experimental
     Region          399..418
                     /gene="NR3C1"
                     /region_name="Domain"
                     /note="Glu/Ser/Pro/Thr-rich (PEST region) (Potential)."
                     /evidence=not_experimental
     Site            421..486
                     /gene="NR3C1"
                     /site_type="DNA binding"
                     /note="Nuclear receptor-type."
                     /evidence=experimental
     Region          421..441
                     /gene="NR3C1"
                     /region_name="Zinc finger region"
                     /note="C4-type."
                     /evidence=experimental
     Region          421
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="C -> Y (in a glucocorticoid resistant leukemia cell
                     line). /FTId=VAR_015631."
                     /evidence=experimental
     Region          451
                     /gene="NR3C1"
                     /region_name="Splicing variant"
                     /note="G -> GR (in isoform Gamma). /FTId=VSP_007363."
                     /evidence=experimental
     Region          457..481
                     /gene="NR3C1"
                     /region_name="Zinc finger region"
                     /note="C4-type."
                     /evidence=experimental
     Region          477
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="R -> H (in glucocorticoid resistance).
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                /FTId=VAR_013472."
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     Region     487..527
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                /region_name="Domain"
                /note="Hinge."
                /evidence=experimental
     Region     491..674
                /gene="NR3C1"
                /region_name="Splicing variant"
                /note="Missing (in isoform GR-A). /FTId=VSP_013340."
                /evidence=experimental
     Region     528..777
                /gene="NR3C1"
                /region_name="Domain"
                /note="Steroid-binding."
                /evidence=experimental
     Region     559
                /gene="NR3C1"
                /region_name="Variant"
                /note="I -> N (in glucocorticoid resistance; interferes
                with translocation to the nucleus and thereby strongly
                reduces transcription activation. Is equally impaired in
                nuclear export. Acts as dominant negative mutant).
                /FTId=VAR_015632."
                /evidence=experimental
     Site       585
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="R->A: Reduces activation mediated by ligand binding
                domain; when associated with A-590."
                /evidence=experimental
     Site       590
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="D->A: Reduces activation mediated by ligand binding
                domain; when associated with A-585."
                /evidence=experimental
     Site       602
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="F->S: Increases solubility. No effect on
                transactivation by dexamethasone."
                /evidence=experimental
     Site       625
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="P->A: Decreases transactivation by dexamethasone by
                95%."
                /evidence=experimental
     Site       628
                /gene="NR3C1"
                /site_type="mutagenized"
                /note="I->A: Decreases dimerization and transactivation by
                dexamethasone; when associated with S-602."
                /evidence=experimental
     Region     641
                /gene="NR3C1"
                /region_name="Variant"
                /note="D -> V (in glucocorticoid resistance).
                /FTId=VAR_004676."
                /evidence=experimental
     Region     679
                /gene="NR3C1"
                /region_name="Variant"
                /note="G -> S (in glucocorticoid resistance; has 50%
                binding affinity). /FTId=VAR_013473."
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                     /evidence=experimental
     Site            703
                     /gene="NR3C1"
                     /site_type="mutagenized"
                     /note="K->R: Slightly reduces sumoylation."
                     /evidence=experimental
     Region          728..777
                     /gene="NR3C1"
                     /region_name="Splicing variant"
                     /note="VVENLLNYCFQTFLDKTMSIEFPEMLAEIITNQIPKYSNGN IKKLLFHQK
                     -> NVMWLKPESTSHTLI (in isoform Beta). /FTId=VSP_003703."
                     /evidence=experimental
     Region          729
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="V -> I (in glucocorticoid resistance).
                     /FTId=VAR_004677."
                     /evidence=experimental
     Region          747
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="I -> M (in glucocorticoid resistance; alters
                     interaction with NCOA2 and strongly reduces transcription
                     activation. Acts as dominant negative mutant).
                     /FTId=VAR_015633."
                     /evidence=experimental
     Region          753
                     /gene="NR3C1"
                     /region_name="Variant"
                     /note="L -> F (in two glucocorticoid resistant leukemia
                     cell lines lacking the normal allele). /FTId=VAR_004678."
                     /evidence=experimental
ORIGIN
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       61 llvdfpkgsv snaqqpdlsk avslsmglym getetkvmgn dlgfpqqgqi slssgetdlk
      121 lleesianln rstsvpenpk ssastavsaa ptekefpkth sdvsseqqhl kgqtgtnggn
      181 vklyttdqst fdilqdlefs sgspgketne spwrsdllid encllsplag eddsfllegn
      241 snedckplil pdtkpkikdn gdlvlsspsn vtlpqvktek edfielctpg vikqeklgtv
      301 ycqasfpgan iignkmsais vhgvstsggq myhydmntas lsqqqdqkpi fnvippipvg
      361 senwnrcqgs gddnltslgt lnfpgrtvfs ngysspsmrp dvssppssss tattgpppkl
      421 clvcsdeasg chygvltcgs ckvffkrave gqhnylcagr ndciidkirr kncpacryrk
      481 clqagmnlea rktkkkikgi qqattgvsqe tsenpgnkti vpatlpqltp tlvsllevie
      541 pevlyagyds svpdstwrim ttlnmlggrq viaavkwaka ipgfrnlhld dqmtllqysw
      601 mflmafalgw rsyrqssanl lcfapdliin eqrmtlpcmy dqckhmlyvs selhrlqvsy
      661 eeylcmktll llssvpkdgl ksqelfdeir mtyikelgka ivkregnssq nwqrfyqltk
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Feb 9 2005 14:31:10

UniProtKB/Swiss-Prot entry P04150

Entry information

Entry name	**GCR_HUMAN**
Primary accession number	**P04150**
Secondary accession number	P04151
Entered in Swiss-Prot in	Release 03, November 1986
Sequence was last modified in	Release 03, November 1986
Annotations were last modified in	Release 47, May 2005

Name and origin of the protein

Protein name	**Glucocorticoid receptor**
Synonym	**GR**
Gene name	**Name: NR3C1** Synonyms: GRL
From	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.

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"Characterization of two novel mutations in the glucocorticoid receptor gene in patients with primary cortisol resistance.";
Clin. Endocrinol. (Oxf.) 55:363-371(2001).

[33] CHARACTERIZATION OF VARIANT GLUCOCORTICOID RESISTANCE ASN-559.
DOI=10.1210/jc.86.11.5600;MEDLINE=21558592;PubMed=11701741 [NCBI, ExPASy, EBI, Israel, Japan]

Kino T., Stauber R.H., Resau J.H., Pavlakis G.N., Chrousos G.P.;
"Pathologic human GR mutant has a transdominant negative effect on the wild-type GR by inhibiting its translocation into the nucleus: importance of the ligand-binding domain for intracellular GR trafficking.";
J. Clin. Endocrinol. Metab. 86:5600-5608(2001).

[34] VARIANT GLUCOCORTICOID RESISTANCE MET-747, AND ALTERED INTERACTION WITH THE COACTIVATOR NCOA2.
DOI=10.1210/jc.87.6.2658;MEDLINE=22045363;PubMed=12050230 [NCBI, ExPASy, EBI, Israel, Japan]
Vottero A., Kino T., Combe H., Lecomte P., Chrousos G.P.;
"A novel, C-terminal dominant negative mutation of the GR causes familial glucocorticoid resistance through abnormal interactions with p160 steroid receptor coactivators.";
J. Clin. Endocrinol. Metab. 87:2658-2667(2002).

Comments

- ***FUNCTION***: Receptor for glucocorticoids (GC). Has a dual mode of action: as a transcription factor that binds to glucocorticoid response elements (GRE) and as a modulator of other transcription factors. Affects inflammatory responses, cellular proliferation and differentiation in target tissues.
- ***SUBUNIT***: Heteromultimeric cytoplasmic complex with HSP90, HSP70, and FKBP5 or another immunophilin, or the immunophilin homolog PPP5C. Upon ligand binding FKBP5 dissociates from the complex and FKBP4 takes its place, thereby linking the complex to dynein and mediating transport to the nucleus, where the complex dissociates *(By similarity)*. Binds to DNA as a homodimer, and as a heterodimer with NR3C2 or the retinoid X receptor. Binds STAT5A and STAT5B homodimers and heterodimers. Interacts with NRIP1, POU2F1, POU2F2 and TRIM28 *(By similarity)*. Interacts with several coactivator complexes, including the SMARCA4 complex, CREBBP/EP300, TADA2L and p160 coactivators such as NCOA2 and NCOA6. Interaction with BAG1 inhibits transactivation.
- ***SUBCELLULAR LOCATION***: Cytoplasmic in the absence of ligand; nuclear after ligand-binding.
- ***ALTERNATIVE PRODUCTS***:

  Alternative splicing [5 named forms]
  Alternative initiation
  Comment: Additional isoforms seem to exist.

  Name **Alpha**
  Synonyms Alpha-A
  Isoform ID P04150-1
  Note: Predominant physiological form. Isoform Alpha-B is produced by alternative initiation at Met-27 of isoform Alpha. Both isoforms exhibit similar subcellular location and nuclear translocation after ligand activation. Isoform Alpha-B appears to be more susceptible to degradation, at least when expressed in mammalian cells, but more effective in transcriptional activation and not in transrepression.
  This is the isoform sequence displayed in this entry.

  Name **Beta**
  Synonyms Beta-A
  Isoform ID P04150-2
  Note: No hormone-binding activity. Widely expressed at low level. Localized largely in the nucleus. Isoform Beta-B is produced by alternative initiation at Met-27 of isoform Beta.
  Features which should be applied to build the isoform sequence: VSP_003703.

Name **Gamma**
Synonyms Alpha-2, Gamma-A, Alpha-2-A
Isoform ID P04150-3
Note: Lower transcriptional activity. Expressed at low level.
Features which should be applied to build the isoform sequence: VSP_007363.

Name **GR-P**
Isoform ID P04150-4
Note: Encoded by exons 2-7 plus several basepairs from the subsequent intron region. Lacks the ligand binding domain. Accounts for up to 10-20% of mRNAs.
The sequence of this isoform is not described.

Name **GR-A**
Isoform ID P04150-5
Note: Lacks exons 5, 6 and 7. Found in glucocorticoid-resistant myeloma patients.
Features which should be applied to build the isoform sequence: VSP_013340.

Comment: At least 4 isoforms, Alpha (shown here), Alpha-B, Beta and Beta-B, are produced by alternative initiation at Met-1 and Met-27. The existence of isoform Alpha and isoform Alpha-B has been proved by mutagenesis. As the sequence environment of the 2 potential ATG initiator codons is the same for the other isoforms, alternative initiation of translation could also occur on these transcripts.

- ***TISSUE SPECIFICITY***: Widely expressed.
- ***DOMAIN***: Composed of three domains: a modulating N-terminal domain, a DNA-binding domain and a C-terminal steroid-binding domain.
- ***PTM***: Increased proteasome-mediated degradation in response to glucocorticoids.
- ***PTM***: Phosphorylated in the absence of hormone; becomes hyperphosphorylated in the presence of glucocorticoid. The Ser-203-phosphorylated form is mainly cytoplasmic, and the Ser-211-phosphorylated form is nuclear. Transcriptional activity correlates with the amount of phosphorylation at Ser-211.
- ***PTM***: Sumoylated; this reduces transcription transactivation.
- ***DISEASE***: Defects in NR3C1 are a cause of glucocorticoid resistance [MIM:138040]; also known as cortisol resistance. It is a hypertensive, hyperandrogenic disorder characterized by increased serum cortisol concentrations. Inheritance is autosomal dominant.
- ***SIMILARITY***: Belongs to the nuclear hormone receptor family. NR3 subfamily.
- ***SIMILARITY***: Contains 1 nuclear receptor DNA-binding domain.

Copyright

Cross-references

X03225; CAA26976.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
X03348; CAA27054.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
U80946; AAB64353.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
U78506; AAB64353.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence]
U78507; AAB64353.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence]
U78508; AAB64353.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence]

EMBL	U78509; AAB64353.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78510; AAB64353.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78511; AAB64353.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78512; AAB64353.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U80947; AAB64354.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] U78506; AAB64354.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78507; AAB64354.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78508; AAB64354.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78509; AAB64354.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78510; AAB64354.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78511; AAB64354.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U78512; AAB64354.1; JOINED. [EMBL / GenBank / DDBJ] [CoDingSequence] U01351; AAA16603.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] AY436590; AAQ97180.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] BC015610; AAH15610.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] M69104; AAA88049.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] M73816; AAA53151.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] S68378; AAB20466.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence] AC005601; AAC34207.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	A93370; QRHUGA. B93370; QRHUGB.
PDB	1M2Z; X-ray; A/D=521-777. [ExPASy / RCSB / EBI] 1NHZ; X-ray; A=500-777. [ExPASy / RCSB / EBI] 1P93; X-ray; A/B/C/D=500-777. [ExPASy / RCSB / EBI] Detailed list of linked structures.
SMR	P04150; 417-491.
IntAct	P04150; -.
TRANSFAC	T00337; -. T01920; -.
Ensembl	ENSG00000113580; Homo sapiens. [Contig view]
Genew	HGNC:7978; NR3C1.
CleanEx	HGNC:7978; NR3C1.
GeneCards	NR3C1.
GeneLynx	NR3C1; Homo sapiens.
GenAtlas	NR3C1.
NIEHS-SNPs	NR3C1.
H-InvDB	HIX0005273; -.
MIM	138040 [NCBI / EBI].
GO	GO:0005737; Cellular component: cytoplasm *(traceable author statement)*. GO:0005759; Cellular component: mitochondrial matrix *(traceable author statement)*. GO:0005634; Cellular component: nucleus *(traceable author statement)*. GO:0004883; Molecular function: glucocorticoid receptor activity *(traceable author statement)*. GO:0003700; Molecular function: transcription factor activity *(traceable author statement)*. GO:0007165; Biological process: signal transduction *(traceable author statement)*. GO:0006366; Biological process: transcription from Pol II promoter *(traceable author statement)*.

	QuickGo view:
SOURCE	NR3C1; Homo sapiens.
InterPro	IPR001409; Glcrtcd_receptor. IPR000536; Hrmon_recept_lig. IPR001723; Stdhrmn_receptor. IPR008946; Str_ncl_receptor. IPR001628; Znf_C4steroid. Graphical view of domain structure.
Pfam	PF02155; GCR; 1. PF00104; Hormone_recep; 1. PF00105; zf-C4; 1. Pfam graphical view of domain structure.
PRINTS	PR00528; GLCORTICOIDR. PR00398; STRDHORMONER. PR00047; STROIDFINGER.
ProDom	PD000035; Znf_C4steroid; 1. [Domain structure / List of seq. sharing at least 1 domain]
SMART	SM00430; HOLI; 1. SM00399; ZnF_C4; 1.
PROSITE	PS00031; NUCLEAR_REC_DBD_1; 1. PS51030; NUCLEAR_REC_DBD_2; 1. PROSITE graphical view of domain structure.
NucleaRDB	P04150; GCR_HUMAN.
HOVERGEN	[Family / Alignment / Tree]
BLOCKS	P04150.
ProtoNet	P04150.
ProtoMap	P04150.
PRESAGE	P04150.
DIP	P04150.
ModBase	P04150.
SWISS-2DPAGE	Get region on 2D PAGE.
UniRef	View cluster of proteins with at least 50% / 90% identity.

Keywords

3D-structure; **Alternative initiation**; **Alternative splicing**; **Disease mutation**; **DNA-binding**; **Nuclear protein**; **Phosphorylation**; **Polymorphism**; **Receptor**; **Steroid-binding**; **Trans-acting factor**; **Transcription**; **Transcription regulation**; **Ubl conjugation**; **Zinc-finger**.

Features

 Feature table viewer

 Feature aligner

Key	From	To	Length	Description	FTId
CHAIN	1	777	777	Glucocorticoid receptor, A-type isoforms.	
CHAIN	27	777	751	Glucocorticoid receptor, B-type isoforms.	
INIT_MET	27	27		For B-type isoforms.	

DOMAIN	1	420	420	Modulating.		
DOMAIN	399	418	20	Glu/Ser/Pro/Thr-rich (PEST region) *(Potential)*.		
DNA_BIND	421	486	66	Nuclear receptor-type.		
ZN_FING	421	441	21	C4-type.		
ZN_FING	457	481	25	C4-type.		
DOMAIN	487	527	41	Hinge.		
DOMAIN	528	777	250	Steroid-binding.		
MOD_RES	113	113		Phosphoserine *(By similarity)*.		
MOD_RES	141	141		Phosphoserine *(By similarity)*.		
MOD_RES	203	203		Phosphoserine.		
MOD_RES	211	211		Phosphoserine.		
MOD_RES	226	226		Phosphoserine *(By similarity)*.		
VARSPLIC	728	777		VVENLLNYCFQTFLDKTMSIEFPEMLAEIITNQIPKYSNG NIKKLLFHQK -> NVMWLKPESTSHTLI (in isoform Beta).	VSP_003703	
VARSPLIC	451	451		G -> GR (in isoform Gamma).	VSP_007363	
VARSPLIC	491	674		Missing (in isoform GR-A).	VSP_013340	
VARIANT	23	23	1	R -> K (in dbSNP:6190) [NCBI/Ensembl].	VAR_014140	
VARIANT	29	29	1	F -> L.	VAR_015628	
VARIANT	65	65	1	F -> V (in dbSNP:6192) [NCBI/Ensembl].	VAR_014622	
VARIANT	112	112	1	L -> F.	VAR_015629	
VARIANT	233	233	1	D -> N.	VAR_015630	
VARIANT	363	363	1	N -> S (may increase sensitivity to exogenously administered glucocorticoids; dbSNP:6195) [NCBI/Ensembl].	VAR_004675	
VARIANT	421	421	1	C -> Y (in a glucocorticoid resistant leukemia cell line).	VAR_015631	
VARIANT	477	477	1	R -> H (in glucocorticoid resistance).	VAR_013472	
VARIANT	559	559	1	I -> N (in glucocorticoid resistance; interferes with translocation to the nucleus and thereby strongly reduces transcription activation. Is equally impaired in nuclear export. Acts as dominant negative mutant).	VAR_015632	[3D]
VARIANT	641	641	1	D -> V (in glucocorticoid resistance).	VAR_004676	[3D]
VARIANT	679	679	1	G -> S (in glucocorticoid resistance; has 50% binding affinity).	VAR_013473	[3D]
VARIANT	729	729	1	V -> I (in glucocorticoid resistance).	VAR_004677	[3D]
VARIANT	747	747	1	I -> M (in glucocorticoid resistance; alters interaction with NCOA2 and strongly reduces transcription activation. Acts as dominant negative mutant).	VAR_015633	[3D]
VARIANT	753	753	1	L -> F (in two glucocorticoid resistant leukemia cell lines lacking the normal allele).	VAR_004678	[3D]
MUTAGEN	1	1		M->T: Abolishes expression of A-type isoforms.		
MUTAGEN	27	27		M->T: Abolishes expression of B-type isoforms.		
MUTAGEN	191	191		F->D: Reduces transactivation by the ADA complex.		
MUTAGEN	193	193		I->D: Reduces transactivation by the ADA		

			complex.
MUTAGEN	194	194	L->A: Strongly reduces transactivation by the ADA complex; when associated with V-224 and F-225.
MUTAGEN	197	197	L->E: Reduces transactivation by the ADA complex.
MUTAGEN	213	213	W->A: Strongly reduces transactivation by the ADA complex.
MUTAGEN	224	224	L->V: Strongly reduces transactivation by the ADA complex; when associated with A-194 and F-225.
MUTAGEN	225	225	L->F: Strongly reduces transactivation by the ADA complex; when associated with A-194 and V-224.
MUTAGEN	235	235	F->L: Strongly reduces transactivation by the ADA complex; when associated with V-236.
MUTAGEN	236	236	L->V: Strongly reduces transactivation by the ADA complex; when associated with L-235.
MUTAGEN	277	277	K->R: Strongly reduces sumoylation. Almost complete loss of sumoylation; when associated with R-293.
MUTAGEN	293	293	K->R: Strongly reduces sumoylation. Almost complete loss of sumoylation; when associated with R-277.
MUTAGEN	585	585	R->A: Reduces activation mediated by ligand binding domain; when associated with A-590.
MUTAGEN	590	590	D->A: Reduces activation mediated by ligand binding domain; when associated with A-585.
MUTAGEN	602	602	F->S: Increases solubility. No effect on transactivation by dexamethasone.
MUTAGEN	625	625	P->A: Decreases transactivation by dexamethasone by 95%.
MUTAGEN	628	628	I->A: Decreases dimerization and transactivation by dexamethasone; when associated with S-602.
MUTAGEN	703	703	K->R: Slightly reduces sumoylation.

Sequence information

Length: **777 AA** [This is the length of the unprocessed precursor]

Molecular weight: **85659 Da** [This is the MW of the unprocessed precursor]

CRC64: **C5C90C9A5DD16AAB** [This is a checksum on the sequence]

```
        10         20         30         40         50         60
MDSKESLTPG REENPSSVLA QERGDVMDFY KTLRGGATVK VSASSPSLAV ASQSDSKQRR

        70         80         90        100        110        120
LLVDFPKGSV SNAQQPDLSK AVSLSMGLYM GETETKVMGN DLGFPQQGQI SLSSGETDLK

       130        140        150        160        170        180
LLEESIANLN RSTSVPENPK SSASTAVSAA PTEKEFPKTH SDVSSEQQHL KGQTGTNGGN

       190        200        210        220        230        240
VKLYTTDQST FDILQDLEFS SGSPGKETNE SPWRSDLLID ENCLLSPLAG EDDSFLLEGN

       250        260        270        280        290        300
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 SNEDCKPLIL PDTKPKIKDN GDLVLSSPSN VTLPQVKTEK EDFIELCTPG VIKQEKLGTV

        310         320         330         340         350         360
 YCQASFPGAN IIGNKMSAIS VHGVSTSGGQ MYHYDMNTAS LSQQQDQKPI FNVIPPIPVG

        370         380         390         400         410         420
 SENWNRCQGS GDDNLTSLGT LNFPGRTVFS NGYSSPSMRP DVSSPPSSSS TATTGPPPKL

        430         440         450         460         470         480
 CLVCSDEASG CHYGVLTCGS CKVFFKRAVE GQHNYLCAGR NDCIIDKIRR KNCPACRYRK

        490         500         510         520         530         540
 CLQAGMNLEA RKTKKKIKGI QQATTGVSQE TSENPGNKTI VPATLPQLTP TLVSLLEVIE

        550         560         570         580         590         600
 PEVLYAGYDS SVPDSTWRIM TTLNMLGGRQ VIAAVKWAKA IPGFRNLHLD DQMTLLQYSW

        610         620         630         640         650         660
 MFLMAFALGW RSYRQSSANL LCFAPDLIIN EQRMTLPCMY DQCKHMLYVS SELHRLQVSY

        670         680         690         700         710         720
 EEYLCMKTLL LLSSVPKDGL KSQELFDEIR MTYIKELGKA IVKREGNSSQ NWQRFYQLTK

        730         740         750         760         770
 LLDSMHEVVE NLLNYCFQTF LDKTMSIEFP EMLAEIITNQ IPKYSNGNIK KLLFHQK
```

P04150 in FASTA format

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BLAST BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

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